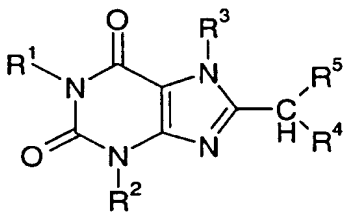
Claims

1. A compound of formula



I

in free or salt form, where

R^1 is hydrogen or alkyl optionally substituted by hydroxy, alkoxy, or alkylthio,

R^2 is hydrogen, alkyl, hydroxyalkyl, alkylcarbonyloxyalkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, cycloalkylalkyl, heterocyclylalkyl, aralkyl in which the aryl ring thereof is optionally fused to a 5-membered heterocyclic group or is optionally substituted by one or more substituents selected from alkoxy, amino, alkylamino, dialkylamino, acylamino, halogen, hydroxy, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, alkylsulfonylamino or dialkylaminosulfonylamino,

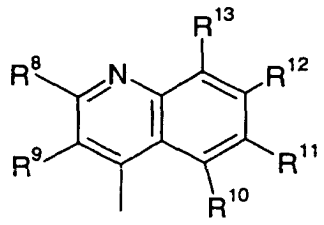
R^3 is hydrogen or alkyl optionally substituted by hydroxy, alkoxy, or alkylthio,

R^4 is hydrogen or alkyl,

R^5 is a quinolinyl, isoquinolinyl or oxodihydroisoquinolinyl group optionally fused to a 5-membered heterocyclic group and optionally substituted by one or more substituents selected from halogen, cyano, hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkoxy, alkylthio, alkenyl, alkoxycarbonyl, alkynyl, carboxyl, acyl, a group of formula -$N(R^6)R^7$, aryl optionally substituted by one or more substituents selected from halogen or alkoxy, or heteroaryl having 5 or 6 ring atoms attached through a ring carbon atom to the indicated carbon atom, and

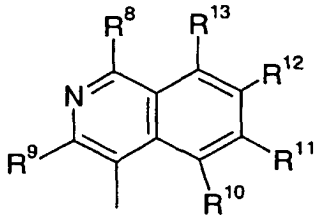
R^6 and R^7 are each independently hydrogen or alkyl optionally substituted by hydroxy or alkoxy or one of R^6 and R^7 is hydrogen and the other is acyl, or R^6 and R^7 together with the nitrogen atom to which they are attached denote a 5- or 6- membered heterocyclyl group.

2. A compound according to claim 1, in which R^5 is a quinolinyl group of formula



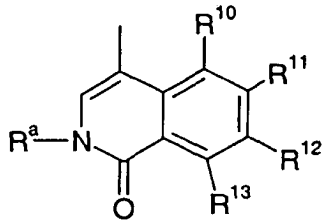
II

or an isoquinolinyl group of formula



III

or an oxodihydroisoquinolinyl group of formula



IIIA

where R^8, R^9, R^{10}, R^{11}, R^{12} and R^{13} are each independently hydrogen or a substituent selected from halogen, cyano, hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkoxy, alkylthio, alkenyl, alkoxycarbonyl, alkynyl, carboxyl, acyl, a group of formula -$N(R^6)R^7$, aryl optionally substituted by one or more substituents selected from halogen or alkoxy, or heteroaryl having 5 or 6 ring atoms, and R^6 and R^7 are as defined in claim 1, or R^{11} and R^{12} together with the carbon atoms to which they are attached denote a 5-membered heterocyclic group having two oxygen or nitrogen atoms in the ring, and R^a is hydrogen or C_1-C_4-alkyl.

3. A compound according to claim 1, in which

R^1 is hydrogen or C_1-C_4-alkyl optionally substituted by hydroxy, C_1-C_4-alkoxy or C_1-C_4-alkylthio,

R^2 is hydrogen, C_1-C_8-alkyl, hydroxy-C_1-C_8-alkyl, C_1-C_4-alkylcarbonylonxy-C_1-C_8-alkyl, C_1-C_4-alkoxy-C_1-C_8-alkyl, or C_1-C_4-alkylthio-C_1-C_8-alkyl, C_2-C_4-alkenyl, C_3-C_8-cycloalkyl-C_1-C_4-alkyl, heterocyclyl-C_1-C_4-alkyl where the heterocyclyl group is a 5- or 6- membered heterocyclyl group having one or two hetero atoms selected from nitrogen and oxygen atoms in the ring, phenyl-C_1-C_4-alkyl in which the phenyl ring is optionally substituted by one or more substituents selected from C_1-C_4-alkoxy, amino, C_1-C_4-alkylamino, di(C_1-C_4-alkyl)amino, C_1-C_4-alkylcarbonylamino, halogen, C_1-C_4-alkylsulfonylamino, or di(C_1-C_4-alkyl)aminosulfonylamino, and is optionally fused to a 5- membered heterocyclic ring having two oxygen or two nitrogen atoms in the ring,

R^3 is hydrogen or C_1-C_4-alkyl optionally substituted by hydroxy, C_1-C_4-alkoxy or C_1-C_4-alkylthio,

R^4 is hydrogen or C_1-C_4-alkyl,

R^5 is a quinolinyl, isoquinolinyl or oxodihydroisoquinolinyl group optionally fused to a 5-membered heterocyclic group having two oxygen or two nitrogen atoms in the ring and optionally substituted by one or more substituents selected from halogen, cyano, carboxy, hydroxy, C_1-C_4-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylthio-C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_1-C_4-alkylcarbonyl, a group -N(R^6)R^7 or phenyl optionally substituted by one or more substituents selected from halogen or C_1-C_4-alkoxy and

R^6 and R^7 are each independently hydrogen or C_1-C_4-alkyl optionally substituted by hydroxy or alkoxy, or one of R^6 and R^7 is hydrogen and the other is C_1-C_4-alkylcarbonyl, or R^6 and R^7 together with the nitrogen atom to which they are attached denote a 5- or 6-membered heterocyclyl group having one or two nitrogen atoms and, optionally, an oxygen atom in the ring.

4. A compound according to claim 2, in which

R^1 is hydrogen or C_1-C_4-alkyl, R^2 is hydrogen, C_1-C_8-alkyl, hydroxy-C_1-C_8-alkyl, or C_1-C_4-alkylcarbonyloxy-C_1-C_8-alkyl, C_2-C_4-alkenyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, heterocyclyl-C_1-C_4-alkyl where the heterocyclyl group is a 5- membered heterocyclyl group having one nitrogen or oxygen atom in the ring, phenyl-C_1-C_4-alkyl in which the phenyl ring is optionally substituted by one or two substituents selected from C_1-C_4-alkoxy, amino, C_1-C_4-alkylcarbonylamino, chlorine, bromine, C_1-C_4-alkylsulfonylamino, or di(C_1-C_4-alkyl)aminosulfonylamino and is optionally fused to a 5- membered heterocyclic ring having two oxygen atoms in the ring,

R^3 is hydrogen or C_1-C_4-alkyl,

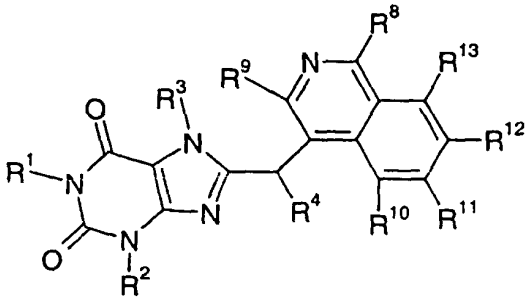
R^4 is hydrogen or C_1-C_4-alkyl,

R^5 is a quinolinyl group of formula II, an isoquinolinyl group of formula III or an oxodihydroisoquinolinyl group of formula IIIA, where R^8, R^9, R^{10}, R^{11}, R^{12} and R^{13} are each independently selected from hydrogen, halogen, cyano, carboxy, hydroxy, C_1-C_4-alkyl, hydroxy-C_1-C_4-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_4-alkylthioC_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_1-C_4-alkylcarbonyl, a group -N(R^6)R^7 or phenyl optionally substituted by one or two substituents selected from halogen or C_1-C_4-alkoxy, or R^{11} and R^{12} together with the carbon atoms to which they are attached denote a 5-membered heterocyclic group having two oxygen atoms in the ring, and

R^6 and R^7 are each independently hydrogen or C_1-C_4-alkyl optionally substituted by hydroxy or alkoxy or one of R^6 and R^7 is hydrogen and the other is C_1-C_4-alkylcarbonyl, or R^6 and R^7 together with the nitrogen atom to which they are attached denote a 6-membered heterocyclyl group having one or two nitrogen atoms, or one nitrogen atom and one oxygen atom, in the ring.

5. A compound according to claim 4, in which R^5 is an isoquinolinyl group of formula III in which R^8 is hydrogen, C_1-C_4-alkyl, halogen, cyano, -N(R^6)R^7 where R^6 and R^7 are each independently C_1-C_4-alkyl or R^6 and R^7 together with the nitrogen atom to which they are attached denote a 6-membered heterocyclyl group having one or two nitrogen atoms, or one nitrogen atom and one oxygen atom, in the ring, or phenyl substituted by one or two C_1-C_4-alkoxy groups; R^9 and R^{10} are each independently hydrogen, C_1-C_4-alkyl or halogen; R^{11} and R^{12} are each independently hydrogen, halogen, cyano, carboxy, hydroxy, C_1-C_4-alkyl, C_1-C_4-alkoxy or C_2-C_4-alkynyl, or R^{11} and R^{12} together with the carbon atoms to which they are attached denote a 5- membered heterocycle having two oxygen atoms in the ring; and R^{13} is hydrogen or halogen.

6. A compound of formula XXXXVI



XXXXVI

in free or salt form, where

(i) R^1 is CH_3, R^2 is $(CH_3)_2CHCH_2$, R^3 and R^4 are each H, R^8 is CH_3, R^9 and R^{10} are each H, and R^{11} and R^{12} are each OCH_3; or

(ii) R^1 is CH_3, R^2 is $(CH_3)_2CHCH_2$, R^3, R^4, R^8, R^9 and R^{10} are each H, and R^{11} and R^{12} are each OCH_3; or

(iii) R^1 is CH_3, R^2 is $(CH_3)_3CCH_2$, R^3, R^4, R^8, R^9 and R^{10} are each H, and R^{11} and R^{12} are each OCH_3; or

(iv) R^1 is CH_3, R^2 is $(CH_3)_2CHCH_2$, R^3, R^4, R^9 and R^{10} are each H, R^8 is Cl and R^{11} and R^{12} are each OCH_3; or

(v) R^1 is CH_3, R^2 is $(CH_3)_2CHCH_2$, R^3, R^4, R^8, R^9 and R^{10} are each H, R^{11} is OCH_3 and R^{12} is H; or

(vi) R^1 is CH_3, R^2 is cyclopropylmethyl, R^3, R^4, R^8, R^9, R^{10} and R^{12} are each H and R^{11} is OCH_3 ; or

(vii) R^1 is CH_3, R^2 is $(CH_3)_2CHCH_2$, R^3, R^4, R^8, R^9, R^{10} and R^{12} are each H and R^{11} is CH $\equiv$C; or

(viii) R^1 is CH_3, R^2 is 4-(N-dimethylaminosulfonylamino)benzyl, R^3, R^4, R^8, R^9 and R^{10} are each H and R^{11} and R^{12} are each OCH_3; or

(ix) R^1 is CH_3, R^2 is $HOCH_2CH(CH_3)CH_2$, R^3, R^4, R^8, R^9 and R^{10} are each H and R^{11} and R^{12} are each OCH_3; or

(x) R^1 is CH_3, R^2 is l-methylcyclopropylmethyl, R^3, R^4, R^8, R^9 and R^{10} are each H and R^{11} and R^{12} are each OCH_3.

7. A compound according to any one of claims 1 to 6 for use as a pharmaceutical.

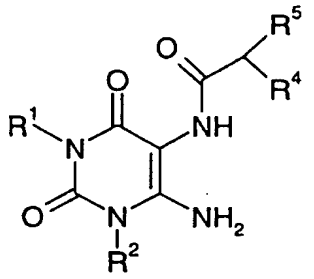
8. A pharmaceutical composition comprising as active ingredient a compound according to any one of claims 1 to 6, optionally together with a pharmaceutically acceptable diluent or carrier.

9. The use of a compound according to any one of claims 1 to 6 for the manufacture of a medicament for the treatment of a condition mediated by PDE5.

10. The use of a compound according to any one of claims 1 to 6 for the manufacture of a medicament for the treatment of sexual dysfunction, particularly male erectile dysfunction.

11. A process for the preparation of a compound of formula I in free or salt form which comprises

1) (a) dehydrating a compound of formula



IV

where R^1, R^2, R^4 and R^5 are as defined in claim 1; or

(b) for the preparation of a compound of formula I in free or salt form where R^3 is alkyl optionally substituted by hydroxy, alkoxy or alkylthio, reacting a compound of formula I in free or salt form with an appropriate alkylating agent; or

(c) for the preparation of a compound of formula I in free or salt form where R^2 is aralkyl substituted in the aryl ring by alkylsulfonylamino or dialkylaminosulfonylamino, reacting a compound of formula I in salt form where R^2 is aralkyl substituted by amino with, respectively, an alkylsulfonyl halide or dialkylaminosulfonyl halide; or

(d) for the preparation of a compound of formula I in free or salt form where R^2 is hydroxy-substituted alkyl, hydration of a compound of formula I where R^2 is alkenyl; or

(e) for the preparation of a compound of formula I in free or salt form where R^2 is alkyl substituted by alkylcarbonyloxy, appropriate esterification of a compound of formula I where R^2 is hydroxy-substituted alkyl; or

(f) for the preparation of a compound of formula I in free or salt form where R^2 is aralkyl substituted in the aryl ring by amino, hydrolysing a compound of formula I where R^2 is aralkyl substituted in the aryl ring by acylamino; or

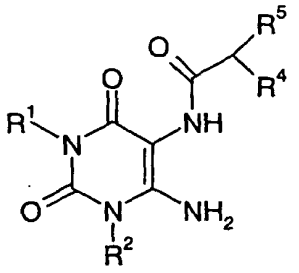
(g) for the preparation of a compound of formula I in free or salt form where R^5 is quinolinyl or isoquinolinyl substituted by hydroxy, dealkylation of a compound of formula I where R^5 is respectively quinolinyl or isoquinolinyl substituted by alkoxy; or

(h) for the preparation of a compound of formula I in free or salt form where R^5 is quinolinyl or isoquinolinyl substituted by halogen, halogenation of a compound of formula I where R^5 is respectively quinolinyl or isoquinolinyl having an unsubstituted ring carbon atom available for halogenation; or

(i) for the preparation of a compound of formula I in free or salt form where R^2 is a cyclopropyl group, optionally substituted by alkyl, subjecting a compound of formula I where R^2 is alkenyl to a Simmons Smith cyclopropanation reaction; and

2) recovering the resulting product of formula I in free or salt form.

12. A compound of formula IV



IV

where R^1, R^2, R^4 and R^5 are as defined in claim 1.